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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

BERTOGLIO, VALARIE E

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

9M.

Office Action Summary

Application No.

09/913,854

Applicant(s)

ANDREWS ET AL.

Examiner

Valarie Bertoglio

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 and 10-25 is/are pending in the application.
- 4a) Of the above claim(s) 19-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 10-18 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 August 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- 1) ☐ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 0504.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 04/26/2004 has been entered. Claim 9 has been canceled. Claims 19-24 are withdrawn. Claims 1-8 and 10-25 are pending and claims 1-8, 10-18 and 25 are under consideration in the instant action.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

In light of applicant's amendment to the claims, the rejection of claims 1-12 under 35 USC 101 is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-8, 10-18 and 25 under 35 U.S.C. 112, first paragraph, is maintained because the specification, while being enabling for a method for preparing a cell culture comprising cells possessing at least one pluripotent characteristic, which cells are cultured from an isolated cell comprising at least part of the cytoplasm from a mammalian embryonic stem cell or mammalian embryonic germ cell combined with a nucleus of a somatic cell, does not reasonably provide enablement for a method of preparing a cell possessing at least one pluripotent characteristic, which cell comprises at least part of the cytoplasm from a

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mammalian embryonal stem cell or mammalian embryonal germ cell combined with a nucleus of a somatic cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant's arguments have been fully considered and are found partially persuasive.

The aspect of the rejection with respect to the specification failing to provide adequate guidance to make the claimed cells wherein the cells are pluripotent is withdrawn in light of applicant's arguments. Applicant has argued that the demonstration of Oct-4 expression in tumor cells fails to negate the use of Oct-4 as an art recognized marker of pluripotency. This argument is deemed persuasive (refer to pages 8-9 of Applicant's response dated 04/26/2004).

In light of applicant's arguments (refer to page 11, paragraph 1 of Applicant's response dated 04/26/2004) with respect to the requirement of an activation step is withdrawn.

The aspect of the rejection set forth on pages 10-11 of the previous rejection is maintained for reasons of record and is applied to claims 1-8, 10-12, 18 and 25 as set forth below. Claim 1 is directed to a single cell derived by the combination of ES or EG cytoplasm with a somatic cell nucleus. Claims 2-8, 10-12, 18 and 25 depend from claim 1. A cell comprising an ES or EG cell cytoplasm and a somatic nucleus cannot have a pluripotent characteristic as it comprises a differentiated somatic nucleus. It is the culture of said combined cell that results in cells comprising a reprogrammed or partially reprogrammed nucleus that is no longer somatic. It is the cells descendent from the combined cell that are demonstrated in the specification to express Oct-4, an example of a pluripotential characteristic, as Oct-4 expression is assessed after 2 days of culture (page 28, lines 9-24). In fact, Oct-4 is an embryonic gene expressed in

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undifferentiated embryonic stem and germ cells. Cells that lose Oct-4 expression differentiate to form various somatic tissues (refer to Pesce, 1998, BioEssays, Vol. 20, pages 722-732) and would not be expected to be expressed from a somatic nucleus transferred to an ES cell cytoplasm. It is thought that Oct-4 has a conserved function in partitioning the germ and soma in vertebrates (see Pesce, throughout and specifically page 723, col. 2, paragraph 2). Accordingly, the specification has demonstrated that Oct-4 was not expressed in mock fused mouse thymocytes cells comprising a somatic nucleus (page 29, lines 1-7). Therefore, one would not expect Oct-4 expression, or any other pluripotential characteristic, from a somatic cell nucleus. Therefore, the specification teaches culturing cells descendent from the combined cell wherein the cells exhibit at least one pluripotential characteristic, which is Oct-4 expression. The specification does not teach that the isolated cell encompassed by the claims expresses Oct-4 or exhibits any other pluripotential characteristic. As such, the specification fails to enable making an isolated cell possessing at least one pluripotential characteristic when the cell comprises ES or EG cytoplasm and a somatic cell nucleus.

Applicant argued the previous rejection of claim 5 that was rejected under similar grounds on pages 10-11 of the previous office action. Applicant argues that the concept of "nuclear transfer" unit is not directly applicable to the present invention. In response, it is a moot point whether the claimed cell derived through nuclear transfer qualifies as a "nuclear transfer unit" as generally accepted by those skilled in the art. The claim as written encompasses a cell with a somatic nucleus; however, the specification demonstrates no pluripotential characteristics in such a cell. The specification teaches Oct-4 expression in cultured cells in which the nucleus has been reprogrammed to an embryonic state.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8,10-18 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection of claim 3 for reciting a latent term is maintained for reasons of record and is applied to claims 1,2 and 10 for reasons set forth below. Claims 1-3 and 10 are unclear because they recite that the cell has “the ability to...” or “has the capacity to”, which is a latent property and not an active property stating that the properties actually do occur. It is unclear whether the characteristic actually occur or if they merely have the potential to occur. Therefore, it is unclear if the latent property is ever obtained.

Applicant has argued that one skilled in the art would understand that the cells must be immortal as they have the ability to proliferate in culture in an undifferentiated state (page 12, paragraph 3).

In response, again, having the “ability” is a latent property that does not actively describe the cells. Both “ability to and capacity to” encompass situations wher the cells do, and do not, possess the ability or capacity. From Applicant’s arguments, it would appear that they mean the active step of having the ability or capacity. If this assumption is true, Applicant should amend the claims, such as in claim 1, to read “...which characteristic is differentiation into at least one selected tissue type”. Claims 4-8, 10,11, 18 and 25 depend from claim 1.

Claim 1 is unclear because it is drawn to an isolated cell comprising the cytoplasm of an ES or EG cell and a somatic cell nucleus. It is unclear if the claim is intended to encompass only the combined cell comprising a nucleus from a somatic cell or if it is meant to encompass cells resulting from culture and expansion of the combined cell comprising a nucleus from a somatic cell. The claim, as written, does not encompass the latter.

Claim 11 is unclear as it is drawn to a cell line comprising cells according to claim 1. Claim 11 is unclear because it states the “cells” of claim 1, however, claim 1 encompasses only a single cell. Claim 12 depends from claim 11.

Claim 13 recites the limitation “said combined cell” in step (ii). There is insufficient antecedent basis for this limitation in the claim. The claim has not established that a “combined cell” results from method step (i).

Claim 13 is unclear because step (iii) refers to “said cell”. It is unclear whether “said cell” is referring to the combined cell resulting from step (i) or to the stem or embryonal germ cell or somatic cell of step (i).

Claim 14 recites the limitation “said cytoplasmic part” in step (iii). There is insufficient antecedent basis for this limitation in the claim. The claim has not established that a “cytoplasmic part” results from method step (ii). Similarly, claim 15 refers to “said cytoplasmic part”

Claim 14 recites the limitation “said combined cell” in step (v). There is insufficient antecedent basis for this limitation in the claim. The claim has not established that a “combined cell” results from method step (iv).

Claim 18 is unclear as it is drawn to a cell culture comprising at least one cell of claim 1. As set forth above, claim 1 encompasses only one cell. Therefore, the culture cannot contain any more than one cell of claim 1.

Claim 25 is unclear as it is drawn to a kit comprising at least one cell of claim 1. As set forth above, claim 1 encompasses only one cell. Therefore, the kit cannot contain any more than one cell of claim 1.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In light of Applicant's amendment to claim 1, the rejection of claims 1-12 and 25 under 35 USC 112 (a) and 112 (b) is withdrawn.

However, a new grounds of rejection appears below.

Claims 1-8, 10-12, 18 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomson [WO 96/22362, published 25 July 1996].

The claims are directed to a cell comprising at least part of the cytoplasm derived from an embryonal stem cell or embryonal germ cell combined with a nucleus of a somatic cell. In further embodiments, the cell has pluripotential characteristics that includes the expression of at least one selected marker of pluripotential cells, the cell can proliferate in continuous culture in an undifferentiated state for at least six months, the cell has the pluripotential characteristic that includes the presence of telomerase activity, and a chromosome methylation pattern characteristic of pluripotential cells, and can induce tumors when introduced into an animal.

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Thomson taught the isolation and purification of primate embryonic stem cells that are capable of indefinite proliferation *in vitro* in an undifferentiated state, are capable of differentiation to derivatives of all three embryonic germ layers, and maintain a normal karyotype throughout prolonged culture. The pluripotent cells are negative for SSEA-1, positive for the SSEA-3 marker, positive for the SSEA-4 marker, TRA-1-60, TRA-1-81 and alkaline phosphatase. Thomson taught that the primate cells can continue to proliferate in an undifferentiated state for at least one year. See p. 7, lines 9-32. Thomson taught that tumors formed after injection of rhesus ES cells into the hindleg muscles of SCID mice [see Figure 5]. The cell of Thomson comprises an embryonic nucleus rather than a somatic nucleus. However, the cell of Thomson and the cell of the instant invention are materially identical and each is indistinguishable from the other. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spade, 911F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433. See the M.P.E.P. 2112.01.

Note further that claim 25 is directed to a kit comprising the cells of claim 1, instructions with respect to maintenance of the cell in culture, and optionally factors required to induce differentiation of the cell into at least one desired tissue type or organ.

In re Gulack (CAFC) 217 USPQ 401 relates to a measuring cup. In the case of *In re* Gulack, the printed matter is considered a patentable distinction because the function of the device depends upon the printed matter itself, which is a part of the substrate; without the printed indicia or numbers, the substrates lose their function. Such is not the case with the instantly claimed kit. The components of the kit remain fully functional absent the printed instructions for use. Thus, the instructions for use included in a kit or article of manufacture constitute "intended use" for that kit or article of manufacture. Intended use does not impart patentable weight to a product. See MPEP 2111.03:

Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. *In re* Casey 370 F.2d 576, 152 USPQ 235 (CCPA 1967); *In re* Otto, 312 F.2d 937, 938, 136 USPQ 458, 459, (CCPA 1963).

In the instant case, claim 25 is drawn to a kit comprising the cells of claim 1, instructions with respect to maintenance of the cell in culture, and optionally factors required to induce differentiation of the cell into at least one desired tissue type or organ. The intended use, which is recited on the instructions, lacks a functional relationship to the kit because the instructions do not physically or chemically affect the chemical nature of the components of the kit, and furthermore, the components of the kit can still be used by the skilled artisan for other purposes (as a whole or individually). Therefore, the kit is unpatentable over the prior art because they function equally effectively with or without the instructions, and accordingly no functional relationship exists between the instructions for use and the kit components.

Accordingly, Thomson anticipates the claimed invention.

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Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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